AMENDMENTS TO THE SPECIFICATION

Please replace paragraph [0088] on page 19 with the following paragraph:

[0088] FIG. 1B is graph of the absorbance spectra for micro-filtered human plasma (line A), 1% aqueous glucose solution (line B), and ultra-filtrated human plasma (line C). The micro-filtered human plasma is donor-grade human plasma obtained from US Biological. The micro-filtered human plasma was filtered through 0.2 μm syringe filter prior to measurement. ~~Ethylene damine~~ Ethylenediamine tetraacetic acid (EDTA) was present as a preservative. The micro-filtered human plasma is known to contain about 90% water and about 10% dissolved proteins, which include coagulation factors that, under certain conditions, may produce a precipitate known as "cryoprecipitate." As illustrated, the micro-filtered human plasma absorbance peaks occur, in decreasing order of magnitude, at 6.47 μm, 6.05 μm, 7.14 μm, 6.87 μm, and 7.60 μm. Of particular interest is the strength of the absorbance signal present in the 9 μm to 10 μm range. While the main absorbance peaks appear not to interfere with glucose measurement in the 9 μm to 10 μm range, the presence of such a high magnitude absorbance signal may still interfere with accurate glucose measurement. Contrast the micro-filtered human plasma absorbance spectra to the ultra-filtrated human plasma (Line C). The ultra-filtration human plasma had been passed through a ultrafiltration membrane having a cut-off at 30 k Dalton (kD) using a commercially available ultrafiltration membrane. As illustrated, the ultra-filtrated human plasma absorbance peaks occur, in decreasing order of magnitude, at about 6.32 μm, about 6.12 μm, about 6.05 μm, about 7.13 μm and about 7.35 μm. It is important to note that the primary absorbance peaks are similar to those in the microfiltrated human plasma, but the absorbance magnitude has been reduced by about one-tenth. More importantly, the magnitude of the absorbance signal present in the glucose measuring range (i.e., 9 μm to 10 μm range) has been diminished to a level well below that of the glucose signal, even using a low magnitude signal such as that obtained from a 1% aqueous glucose sample. Thus, FIG. 1B illustrates how the use of appropriately sized physical filtration (i.e., ultrafiltration instead of microfiltration) may be used to minimize the impact of a material on glucose measurement.

Please replace paragraph [0089] beginning with the following paragraph:

[0089] FIG. 1C is graph of the absorbance spectra for a lactate ringer's solution (LRS) (Line A) and a 1% aqueous glucose solution (line B). The LRS solution contains sodium lactate (0.3%) and chlorides of sodium (0.6%), potassium (0.03%) and calcium (0.02%). The LRS absorbance spectrum has multiple peaks because of the presence of the other salts. It is believed that the sodium lactate absorbance peaks occur, in decreasing order of magnitude, at about 6.34 μm, about 8.89 μm, about 9.59 μm, and about 7.61 μm. In this case, the sodium lactate has a number of absorbance peaks in close proximity to some of the glucose absorbance peaks. However, in this example, the likelihood of interference from the LRS solution is diminished by advantageously selecting the glucose peak centered at about 9.32 μm. The selection of a particular spectra of interest is accomplished, for example, through the optimal selection of an ~~infra-red~~ infrared (IR) emitter having a radiation signal in the wavelength range of interest (here, mid infrared) alone or in combination with the use of a detector with filters for the wavelength or wavelength range of interest. As a result of this technique, the LRS spectrum has little or no impact on detecting and measuring glucose, thereby increasing the accuracy and ease of measuring the glucose spectra. Thus, the advantageous combination of selection of a particular wavelength for glucose monitoring and selective filtering of the absorbance spectra may be employed to obtain glucose measurements more readily and accurately.

Please replace paragraph [00100] with the following paragraph:

[00100] Now referring to FIG. 5A, there is shown another example of a sensor 66 which can be utilized in the methods described herein. Sensor 66 includes a miniature pulsable infrared emitter source 68 with a parabolic reflector. An example of a miniature pulsable infrared emitter source 68 which can be utilized with the methods described herein is commercially available from Ion Optics, which is located in Waltham, Mass. Source 68 includes an electrically coupled infrared source power supply and modulator circuit 74. An example of a power supply and modulator circuit 74 which can be utilized with the methods described herein is commercially available from Boston Electronics, located in Brookline, Mass. Sensor 66 also includes a multi-channel miniature pyroelectric infrared detector 70. Detector 70 includes an electrically coupled pyroelectric detector preamplifier and signal processing circuit 76. An example of a multi-channel miniature pyroelectric infrared detector 70 which can be utilized with the methods described herein is commercially available from InfraTec GmbH, located in Dresden, Germany.

Additional infrared detectors which can be utilized in the methods described herein are commercially available from Wilkes Enterprise, Inc. located in South Norwalk, Conn. Sensor 66 further includes a biological sample cell 78 interposed between source 68 and detector 70. Cell 78 has a sample space 72 defined therein so that a biological fluid can be advanced there through in the direction indicated by arrow 88. For example, a biological fluid such as capillary filtrate collected from a capillary filtrate collector. One capillary filtrate collector which can be utilized in the methods described herein is described by Ash S. R. et al. in U.S. Pat. No. 4,777,953 issued, Oct. 18, 1988 entitled "Capillary filtration and collection method for long-term monitoring of blood constituents," U.S. Pat. No. 4,854,322 issued, Aug. 8, 1989 entitled "Capillary Filtration Collection Device for Long Term Monitoring of Blood Constituents," U.S. Pat. No. 5,002,054 issued, Mar. 26, 1991 entitled "Interstitial Filtration and Collection Device and Method for Long-Term Monitoring of Physiological Constituents of the Body," and "Subcutaneous Ultrafiltration Fibers for Chemical Sampling of Blood: The Capillary Filtrate Collector (CFC)" in Leung WW-F. ed. Proceedings of the National Meeting of the American Filtration Society. Chicago: Advances in Filtration and Separation Technology, Vol. 7, 1993:316-319, which are incorporated herein by reference. The Capillary Filtrate Collector (CFC) contains three looped hollow fiber ultrafiltration membranes (polyacrylonitrile (PAN), 30,000 mw cutoff) placed into the subcutaneous space (FIG. 1). When placed under vacuum, these fibers create an ultrafiltrate which passes from surrounding capillaries, through the fibers, into a polyurethane tubing surrounded by a 2 mm expanded ~~poly tetra fluoro ethylene~~ poly(tetrafluoroethylene) (PTFE) cuff, through the skin, past a "Y" connector with one limb leading to a sampling port, and through a hub and needle into a Vacutainer® providing 55 mm vacuum. Gas also is drawn from the capillaries, creating spaces between ultrafiltrate samples as they move through the tubing. Animal studies have confirmed that the concentration of glucose within the CFC ultrafiltrate is exactly the same as the plasma free water concentration when the filtrate is created. The same is true for a variety of drugs and organics of less than 3000 molecular weight. During operation of sensor 66, source 68 generates a low frequency infrared electromagnetic radiation pulse. Circuit 74 is configured to optimize the signal-to-noise ratio of the pulse reaching the biological fluid contained within sample space 72. The radiation is transmitted through sample space 72 and thus passes through the biological fluid contained therein. As previously discussed, certain wavelengths of the radiation are absorbed by organic substances contained within the biological fluid 34 as the radiation passes there through. The

radiation then interacts with detector 70 which is configured so that only the select wavelength bands and the select reference wavelength band are substantially detected by detector 70. Upon detecting the select wavelength bands and the select reference wavelength band an electrical signal is sent to circuit 76 which processes the electrical signal with a mathematical model to provide a useful measurement of the amount of the organic substance of interest contained within the biological fluid. Note that circuit 76 has a frequency synchronization connection 90 that ensures that high signal-to-noise ratios are maintained through modulated signal detection.

Please replace paragraph [00120] with the following paragraph:

[00120] Since removing protein is intended to remove interfering absorbances, removal of all proteins larger than the substance being measured is desired. In one embodiment at least 80% of the proteins are removed prior to passing the infrared signal through the sample. In another embodiment at least 96% of the proteins are removed prior to passing the infrared signal through the sample. In another embodiment at least 98% of the proteins are removed prior to passing the infrared signal through the sample. Similar removal rates are preferred if the large interfering substance is a material other than a protein (such as ~~deoxyribo nucleic acid~~ deoxyribonucleic acid (DNA) or a large carbohydrate). FIG. 5D provides an exemplary illustration of filtering a sample inside a subcutaneous location of a patient. It is to be appreciated that the biological sample 555 may be filtered outside patient body or at any of a variety of locations prior to passing an infrared signal through the sample.

Please replace paragraph [00155] with the following paragraph:

[00155] This ~~a~~ second modulation technique is particularly useful in determining the overall operational status of the biological sampling and measurement apparatus 500. Regular readings from the second modulation technique may also be utilized to determine the presence and magnitude of the gain shifts in the emitter/sample cell/detector system whenever such gain shifts occur. The ability to detect and compensate for shifts in instrument readings is especially important when the biological sampling and measurement apparatus 500 is used for continuous glucose monitoring. The use of the-second modulated technique allows the system to inform the user that a particular sample may have, for example, an erroneous reading or that some system component has failed or is not performing according to specifications. In one embodiment of the present invention, the radiation absorbing material is placed in the optical pathway of the system

once about every 12 seconds. In another alternative embodiment, the radiation absorbing material is placed in the optical pathway about once every second. In yet another embodiment, the radiation absorbing material is placed in the optical pathway at any time interval sufficient to provide a useful reference measurement. The radiation absorbing material can be reinserted as needed to provide results of the desired accuracy. The radiation absorbing material needs to stay in place for a time sufficient for a measurement to be made. In one embodiment, measurements can be made in a time span of 0.3 second. Longer or shorter second modulation times can be used for other apparatuses; depending on their operating characteristics. It is to be appreciated that in embodiments of the present invention the emitter modulation and the second modulation technique can be used in conjunction to provide a double modulation mode for the emitter/detector system. Any of the emitter modulations may be used with any of the second modulations.

Please replace paragraph [00164] with the following paragraph:

[00164] ~~$C_g = P_0 + P_1 IA_{\lambda,1} + P_2 IA_{\lambda,2} + P_3 IA^2_{\lambda,1} + P_4 IA^2_{\lambda,2} + P_5 IA_{\lambda,1} IA_{\lambda,2}$ (equ. 2)~~

$C_g = P_0 + P_1 IAR_{\lambda,1} + P_2 IAR_{\lambda,2} + P_3 IAR^2_{\lambda,1} + P_4 IAR^2_{\lambda,2} + P_5 IAR_{\lambda,1} IAR_{\lambda,2}$ (equ. 2)

Please replace paragraph [00165] with the following paragraph:

[00165] where (i) Cg is the mean-centered concentration of glucose in the sample measured using methods other than IR absorption, (ii) P1 are calibration constants, and (iii) ~~$IA_{\lambda,j}$~~ $IAR_{\lambda,j}$ is a mean-centered integrated absorbance ratio of two of the selected infrared wavelength bands and the selected reference wavelength band. As previously mentioned, in this equation the variables are mean-centered. The values of the calibration constants are calculated by Matlab 6.1.0.450 release 12.1, the MathWorks Inc. utilizing the following code: (Matlab code omitted.)